



Figure 1 Effects of Dietary Nitrate Supplementation on Endothelial Function, Vascular Stiffness, and Blood Pressure

Dietary nitrate supplementation improved endothelial function as determined by flow-mediated dilation (FMD), reduced vascular stiffness as assessed by augmentation index (Aix@75bpm) and aortic pulse wave velocity (PWV), and lowered systolic blood pressure (SBP). Carotid intima-media thickness (IMT) and diastolic blood pressure (DBP) remained unaffected. Values are presented as mean ± SEM. *p < 0.05 (n = 10 and n = 11, respectively).

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REFERENCES

1. Kaess BM, Rong J, Larson MG, et al. Aortic stiffness, blood pressure progression, and incident hypertension. *JAMA* 2012;308:875-81.
2. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;336:1117-24.

3. Larsen FJ, Ekblom B, Sahlin K, Lundberg JO, Weitzberg E. Effects of dietary nitrate on blood pressure in healthy volunteers. *N Engl J Med* 2006;355:2792-3.
4. Hendgen-Cotta UB, Luedike P, Totzeck M, et al. Dietary nitrate supplementation improves revascularization in chronic ischemia. *Circulation* 2012;126:1983-92.
5. Rassaf T, Heiss C, Mangold S, et al. Vascular formation of nitrite after exercise is abolished in patients with cardiovascular risk factors and coronary artery disease. *J Am Coll Cardiol* 2010;55:1502-3.

Letters to the Editor

Prognostic Stratification of Patients With Vasospastic Angina



I read with interest the report by Takagi et al (1). I was very impressed by the amount of information they were able to gather about a topic that is not frequently seen by any individual practitioner. I congratulate the authors for trying to assess the risk of vasospastic angina by developing a risk score.

I have 1 concern regarding the risk score: the history of out-of-hospital cardiac arrest. Although I admit this is a risk for a future event, it is also an endpoint for a major adverse cardiac event, and I am not sure it belongs in the same category as smoking, angina at rest, organic coronary stenosis, multivessel spasm, ST-segment elevation during angina, and beta-blocker use.

I also noticed that the degree of an acute myocardial infarction did not seem to make any difference in terms of prognosis. Acute myocardial infarction is also an endpoint for a major adverse cardiac event.

The only other issue I have with this well-written, interesting article is that in the first paragraph, the authors seem to equate vasospastic angina with Prinzmetal angina or variant angina. I have no doubt that the cause of the problem for the majority of patients with Prinzmetal angina is coronary artery spasm, but not all ST-segment elevation is related to the spasm. In fact, Prinzmetal (2) described this syndrome before Mason Sones (3) wrote about his experience with selective coronary angiography.

Another point that I think is useful to understand is that this is a relatively recent experience with vasospastic angina, and thus these patients were probably exposed to contemporary aggressive medical management, including lipid reduction, blood pressure control, and aspirin therapy.

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REFERENCES

1. Takagi Y, Takahashi J, Yasuda S, et al. Prognostic stratification of patients with vasospastic angina. *J Am Coll Cardiol* 2013;62:1144-53.
2. Prinzmetal M, Kenamer R, Merliss R, Wada T, Bor N. Angina pectoris. I. A variant form of angina pectoris; preliminary report. *Am J Med* 1959;27:375-88.
3. Sones FM Jr, Shirey EK. Cine coronary arteriography. *Mod Concepts Cardiovasc Dis* 1962;31:735-8.

Reply

Prognostic Significance of Patients With Vasospastic Angina



We thank Dr. Conti for his interest in our recent work (1). Indeed, to the best of our knowledge, this is the first risk score for vasospastic angina (VSA), which is based on our experience with 1,429 patients registered with the Japanese Coronary Spasm Association (JCSA). We previously reported the prognostic significance of out-of-hospital cardiac arrest (OHCA) in our JCSA registry study (2) and the clinical importance and safety of provocation tests of coronary artery spasm (3).

First, Dr. Conti pointed out that a history of OHCA is an endpoint for a major cardiac event in addition to a future event.

Although we fully agree, we also would like to point out that a substantial portion of patients with OHCA have survived without neurological deficits in the current era because of increasing use of bystander cardiopulmonary resuscitation, use of implantable cardioverter-defibrillators, and hypothermia therapy and that a higher portion of these patients are found to have coronary spasm, at least in Japan (4). Thus, we included OHCA in our stratification analysis and found that it is indeed the most significant prognostic factor (1).

Second, Dr. Conti pointed out that we should be careful not to confuse VSA with Prinzmetal angina or variant angina because Prinzmetal described this syndrome before the development of coronary angiography. Although we take this comment well, it is generally accepted that Prinzmetal angina with ST-segment elevation during angina at rest is caused by coronary spasm (but not by nothing else) as a central form of VSA.

Third, Dr. Conti mentioned that the patients with VSA in the JCSA registry were exposed to contemporary aggressive medical management, including lipid reduction, blood pressure control, and aspirin therapy. Indeed, this is the case. We would like to emphasize that our novel risk score for VSA is useful for prognostic stratification of not only Japanese patients, but also Western patients, as we noted in a recent interview (5).

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REFERENCES

1. Takagi Y, Takahashi J, Yasuda S, et al. Prognostic stratification of patients with vasospastic angina. *J Am Coll Cardiol* 2013;62:1144-53.
2. Takagi Y, Yasuda S, Tsunoda R, et al. Clinical characteristics and long-term prognosis of vasospastic angina patients who survived out-of-hospital cardiac arrest: multicenter registry of the Japanese Coronary Spasm Association. *Circ Arrhythm Electrophysiol* 2011;4:295-302.
3. Takagi Y, Yasuda S, Takahashi J, et al. Clinical implications of provocation tests for coronary artery spasm: safety, arrhythmic complications and prognostic impact: multicenter Registry Study of the Japanese Coronary Spasm Association. *Eur Heart J* 2013;34:258-67.
4. Takagi Y, Yasuda S, Takahashi J, et al. Importance of dual induction tests for coronary vasospasm and ventricular fibrillation in patients surviving out-of-hospital cardiac arrest. *Circ J* 2009;73:767-9.
5. Shimokawa H. A novel risk score for predicting MACE in patients with vasospastic angina. *CardioExchange*. Available at: <http://www.cardioexchange.org/voices/a-novel-risk-score-for-predicting-mace-in-japanese-vasospastic-angina-patients/>. Accessed October 7, 2013.